

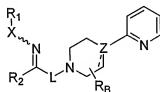
# AMENDMENTS TO THE CLAIMS – Marked Up Version

Claims 1-40, 42-63 and 65-96 are pending in the application. Claims 1-11, 18-20, 32-38, 40-48, 53, 54 and 63-69 have been elected for prosecution. Claims 12-17, 21-31, 39, 49-52, 55-62 and 70-96 have been withdrawn as being drawn to non-elected inventions. Claims 2, 40-48, 53, 54, and 63-69 have been cancelled.

Claims 5, 18, and 33 are currently amended. Claims 34, 35, 36 and 38 are withdrawn.

The following list of claims will replace prior versions and listing of claims in the application:

1. (Previously Amended) A compound of formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein

X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

R<sub>1</sub> is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl; wherein the heteroaryl and the heteroaryl moiety of the heteroarylalkyl are monocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

L is C<sub>1</sub>-C<sub>2</sub> alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R<sub>B</sub> is hydrogen or alkyl;

Z is N; and

--- is absent

2. (Cancelled) The compound according to claim 1 wherein R<sub>3</sub> is



3. (Previously Amended) The compound according to claim 1 wherein  
X is O; and R<sub>2</sub> is aryl.

4. (Previously Amended) The compound according to claim 3 wherein  
R<sub>2</sub> is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen.

5. (Currently Amended) The compound according to claim 1 selected from the group consisting of

(1E)-1-(3-chlorophenyl)-3-(4-pyridin-2-yl-piperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-yl-piperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(4-chlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-(3,4-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,4-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3-chloro-4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-chloro-4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(3,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1Z)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1E)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

3-[(1E)-N-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propanimidoyl]benzonitrile

3-[(1Z)-N-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propanimidoyl]benzonitrile  
(1E)-1-(2,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(2,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-propyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-propyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-allyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-allyloxime;

(1E)-1-(3,5-difluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,5-difluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

({{1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propylidene}amino}oxy)acetonitrile;

1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-butyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-isopropyloxime;

(1E)-1-(3,5-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,5-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-chloro-3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chloro-3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(2-naphthyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(2-naphthyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1Z)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-(2,2,2-trifluoroethyl)oxime;

1-(4-chlorophenyl)-3-(methoxyamino)-2-[(4-pyridin-2-ylpiperazin-1-yl)methyl]propan-1-one O-methyloxime;

(1E)-1-(3,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(2-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(2-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(2,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(2,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-bromophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-bromophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone oxime;

(1Z)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone oxime;

2-{4-[(3E)-3-(hydroxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;

(1E)-1-(4-fluorophenyl)-2-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]ethanone O-methyloxime;

(1Z)-1-(4-fluorophenyl)-2-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-3-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]propan-1-one O-methyloxime;

1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-(2-hydroxyethyl)oxime;

(1E)-1-(4-chlorophenyl)-2-hydroxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-2-hydroxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-chlorophenyl)-2-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime; and

(1Z)-1-(4-chlorophenyl)-2-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime.

6. (Previously Amended) The compound according to claim 1 wherein  
X is O; and R<sub>2</sub> is arylalkyl.

7. (Previously Amended) The compound according to claim 6 wherein  
R<sub>2</sub> is benzyl.

8. (Original) The compound according to claim 7 selected from the group consisting of  
(2E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)acetone O-methyloxime; and  
(2Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)acetone O-methyloxime.

9. (Previously Amended) The compound according to claim 1 wherein  
X is O; and R<sub>2</sub> is heteroaryl.

10. (Previously Amended) The compound according to claim 9 wherein  
R<sub>2</sub> is pyridin-3-yl.

11. (Previously Amended) The compound according to claim 1 selected from the  
group consisting of

(1E)-1-pyridin-3-yl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime; and

(1Z)-1-pyridin-3-yl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime.

12. (Withdrawn) The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is aryl;

Z is C;

--- is a single bond; and

R<sub>4</sub> is heteroaryl.

13. (Withdrawn) The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is C;

--- is a single bond; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

14. (Withdrawn) The compound according to claim 13 selected from the group consisting of

1-(4-fluorophenyl)-3-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]propan-1-one O-methyloxime;

(1E)-1-(4-chlorophenyl)-2-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]ethanone O-methyloxime;

(1Z)-1-(4-chlorophenyl)-2-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-(3-methyl-3',6'-dihydro-2,4'-bipyridin-1'(2'H)-yl)propan-1-one O-methyloxime; and

(1Z)-1-(4-chlorophenyl)-3-(3-methyl-3',6'-dihydro-2,4'-bipyridin-1'(2'H)-yl)propan-1-one O-methyloxime.

15. (Withdrawn) The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is aryl;

Z is CH<sub>3</sub>;

--- is absent; and

R<sub>4</sub> is heteroaryl.

16. (Withdrawn) The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH<sub>3</sub>;

--- is absent; and



R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

17. (Withdrawn) The compound according to claim 16 selected from the group consisting of

(1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

2-{1-[(3E)-3-(4-chlorophenyl)-3-(methoxyimino)propyl]piperidin-4-yl}pyridinium N-oxide;

2-{1-[(3Z)-3-(4-chlorophenyl)-3-(methoxyimino)propyl]piperidin-4-yl}pyridinium N-oxide;

2-{1-[(2E)-2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-4-yl}pyridinium N-oxide; and

2-{1-[(2Z)-2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-4-yl}pyridinium N-oxide.

18. (Currently Amended) The compound according to claim 1 wherein

X is NR<sub>A</sub>; and

R<sub>2</sub> is aryl;

19. (Previously Amended) The compound according to claim 18 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen.

20. (Previously Amended) The compound according to claim 1 that is 1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone methylhydrazone.

21. (Withdrawn) The compound according to claim 2 wherein

X is  $\text{NR}_A$ ;

$\text{R}_2$  is aryl;

Z is CH;

--- is absent; and

$\text{R}_4$  is heteroaryl.

22. (Withdrawn) The compound according to claim 2 wherein

X is  $\text{NR}_A$ ;

$\text{R}_2$  is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH;

--- is absent; and

$\text{R}_4$  is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

23. (Withdrawn) The compound according to claim 22 that is 1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperidin-1-yl)ethanone methylhydrazone.

24. (Withdrawn) The compound according to claim 1 wherein  $\text{R}_3$  is



25. (Withdrawn) The compound according to claim 24 wherein

$\text{R}_2$  is aryl; and

$\text{R}_4$  is heteroaryl.

26. (Withdrawn) The compound according to claim 24 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

27. (Withdrawn) The compound according to claim 26 selected from the group consisting of

1-(4-fluorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-methyloxime;

1-(4-fluorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-ethyloxime;

1-(4-fluorophenyl)-3-(3-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

1-(4-chlorophenyl)-3-(3-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-methyloxime;

2-{1-[2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-3-yl}pyridinium N-oxide; and

2-{1-[3-(4-fluorophenyl)-3-(methoxyimino)propyl]piperidin-3-yl}pyridinium N-oxide.

28. (Withdrawn) The compound according to claim 1 wherein R<sub>3</sub> is



29. (Withdrawn) The compound according to claim 28 wherein

R<sub>2</sub> is aryl; and

R<sub>4</sub> is heteroaryl.

30. (Withdrawn) The compound according to claim 28 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

31. (Withdrawn) The compound according to claim 30 selected from the group consisting of

(1E)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone O-methyloxime;

(1Z)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone O-methyloxime;

(1E)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one oxime;

(1Z)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one oxime;

and

(1Z)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone oxime.

32. (Previously Amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) according to claim 1 in combination with a pharmaceutically acceptable carrier.

33. (Currently Amended) A method of treating male sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a

compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with a pharmaceutically acceptable carrier.

34. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with a phosphodiesterase 5 inhibitor.

35. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with an adrenergic receptor antagonist.

36. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with a dopamine agonist.

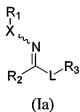
37. (Previously Amended) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof.

38. (Withdrawn Amended) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof.

39. (Withdrawn) A method of treating cardiovascular disorders, inflammatory disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal

comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof.

40. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia)



or a pharmaceutically acceptable salt or ~~prodrug~~ thereof, wherein

X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

R<sub>1</sub> is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl; wherein the heteroaryl and the heteroaryl moiety of the heteroarylalkyl are monocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

R<sub>3</sub> is



R<sub>4</sub> is heteroaryl; wherein the heteroaryl is a monocyclic, five or six membered ring containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R<sub>B</sub> is alkyl;

Z is N; and  
 --- is absent or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

41. (Cancelled) The method according to claim 40 wherein R<sub>3</sub> is



42. (Cancelled) The method according to claim 40 wherein

X is O;

R<sub>2</sub> is aryl;

and

R<sub>4</sub> is heteroaryl.

43. (Cancelled) The method according to claim 40 wherein

X is O;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

44. (Cancelled) The method according to claim 43 where the compound of formula (1a) is selected from the group consisting of

(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2yl)piperazin-1-yl)butan-1-one oxime;

(1Z)-1-(4-fluorophenyl)-4-(4-pyridin-2yl)piperazin-1-yl)butan-1-one oxime;

(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2yl)piperazin-1-yl)butan-1-one

methyloxime; and

(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2-ylpiperazin-1-yl)butan-1-one  
methyloxime.

45. (Cancelled) The method according to claim 40 wherein

X is O;

R<sub>2</sub> is arylalkyl;

and

R<sub>4</sub> is heteroaryl.

46. (Cancelled) The method according to claim 40 wherein

X is O;

R<sub>2</sub> is arylalkyl wherein the arylalkyl is benzyl;

and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-  
2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

47. (Cancelled) The method according to claim 40 wherein

X is O;

R<sub>2</sub> is heteroaryl;

and

R<sub>4</sub> is heteroaryl.

48. (Cancelled) The method according to claim 40 wherein

X is O;

R<sub>2</sub> is heteroaryl wherein the heteroaryl is pyridin-3-yl;

and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-  
2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.



49. (Withdrawn)      The method according to claim 41 wherein
- X is O;
  - R<sub>2</sub> is aryl;
  - Z is C;
  - is a single bond; and
  - R<sub>4</sub> is heteroaryl.
50. (Withdrawn)      The method according to claim 41 wherein
- X is O;
  - R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;
  - Z is C;
  - is a single bond; and
  - R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
51. (Withdrawn)      The method according to claim 41 wherein
- X is O;
  - R<sub>2</sub> is aryl;
  - Z is CH;
  - is absent; and
  - R<sub>4</sub> is heteroaryl.
52. (Withdrawn)      The method according to claim 41 wherein
- X is O;
  - R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;
  - Z is CH;

--- is absent; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

53. (Cancelled) The method according to claim 40 wherein

X is NR<sub>A</sub>;

R<sub>2</sub> is aryl;

and

R<sub>4</sub> is heteroaryl.

54. (Cancelled) The method according to claim 40 wherein

X is NR<sub>A</sub>;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

55. (Withdrawn) The method according to claim 41 wherein

X is NR<sub>A</sub>;

R<sub>2</sub> is aryl;

Z is CH;

--- is absent; and

R<sub>4</sub> is heteroaryl.

56. (Withdrawn) The method according to claim 41 wherein

X is NR<sub>A</sub>;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH;

--- is absent; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

57. (Withdrawn) The method according to claim 41 wherein R<sub>3</sub> is



58. (Withdrawn) The method according to claim 57 wherein

R<sub>2</sub> is aryl; and

R<sub>4</sub> is heteroaryl.

59. (Withdrawn) The method according to claim 57 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

60. (Withdrawn) The method according to claim 40 wherein R<sub>3</sub> is



61. (Withdrawn) The method according to claim 60 wherein

R<sub>2</sub> is aryl; and

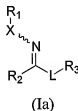
R<sub>4</sub> is heteroaryl.

62. (Withdrawn) The method according to claim 60 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

63. (Cancelled) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (Ia)



or a pharmaceutically acceptable salt thereof, wherein

X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

R<sub>1</sub> is selected from the group consisting of hydrogen, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl; wherein the heteroaryl and the heteroaryl moiety of the heteroarylalkyl are monocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

R<sub>3</sub> is



R<sub>4</sub> is heteroaryl; wherein the heteroaryl is a monocyclic, five or six membered ring containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R<sub>B</sub> is alkyl;

Z is N; and

--- is absent;

in combination with a pharmaceutically acceptable carrier.

64. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

65. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof in combination with a phosphodiesterase 5 inhibitor.

66. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof in combination with an adrenergic receptor antagonist.

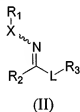
67. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof in combination with a dopamine agonist.

68. (Cancelled) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof.

69. (Cancelled) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof.

70. (Withdrawn) A method of treating cardiovascular disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof.

71. (Withdrawn) A compound of formula (II)



or a pharmaceutically acceptable salt or prodrug thereof, wherein

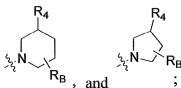
X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

R<sub>1</sub> is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

R<sub>3</sub> is selected from the group consisting of



R<sub>4</sub> is aryl;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl; and

R<sub>B</sub> is selected from the group consisting of hydrogen and alkyl.

72. (Withdrawn) The compound according to claim 70 wherein R<sub>3</sub> is



73. (Withdrawn) The compound according to claim 72 wherein

R<sub>2</sub> is aryl; and

R<sub>4</sub> is aryl.

74. (Withdrawn) The compound according to claim 72 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R<sub>4</sub> is aryl wherein the aryl is phenyl substituted with 0 or 1 substituent selected from the group consisting of alkoxy, cyano, and haloalkyl.

75. (Withdrawn) The compound according to claim 74 selected from the group consisting of

(1E)-1-(4-fluorophenyl)-3-{3-[3-(trifluoromethyl)phenyl]pyrrolidin-1-yl}propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-{3-[3-(trifluoromethyl)phenyl]pyrrolidin-1-yl}propan-1-one O-methyloxime;

1-(4-fluorophenyl)-3-[3-(2-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-3-[3-(3-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-[3-(3-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-3-[3-(4-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime; and

(1Z)-1-(4-fluorophenyl)-3-[3-(4-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime.

76. (Withdrawn) The compound according to claim 70 wherein  $R_3$  is



77. (Withdrawn) The compound according to claim 76 wherein

$R_2$  is aryl; and

$R_4$  is aryl.

78. (Withdrawn) The compound according to claim 76 wherein

$R_2$  is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

$R_4$  is aryl wherein the aryl is phenyl substituted with 0 or 1 substituent selected from the group consisting of alkoxy, cyano, and haloalkyl.

79. (Withdrawn) The compound according to claim 78 selected from the group consisting of

1-(4-fluorophenyl)-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime;

1-phenyl-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime; and



1-(4-chlorophenyl)-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime.

80. (Withdrawn) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (II) in combination with a pharmaceutically acceptable carrier.

81. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

82. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.

83. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.

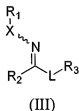
84. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.

85. (Withdrawn) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof.

86. (Withdrawn) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof.

87. (Withdrawn) A method of treating cardiovascular disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof.

88. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to said mammal in need of such treatment a therapeutically effective amount of a compound of formula (III)



or a pharmaceutically acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

R<sub>1</sub> is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

R<sub>3</sub> is



R<sub>4</sub> is aryl;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R<sub>B</sub> is selected from the group consisting of hydrogen and alkyl;

Z is selected from the group consisting of C and CH; and

--- is absent or a single bond provided that when Z is C then --- is a single bond.

89. (Withdrawn) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (III) in combination with a pharmaceutically acceptable carrier.

90. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

91. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.

92. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.

93. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.

94. (Withdrawn) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.

95. (Withdrawn) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.

96. (Withdrawn) A method of treating cardiovascular disorders, inflammatory disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.